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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,494	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/29/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's preliminary amendment filed on 01 February 2002 is acknowledged and entered. Following the amendment, the original claims 1-39 are canceled, and the new claims 40-59 are added.

Currently, claims 40-59 are pending and under consideration.

Formal Matters:

Priority

This application claims priority to US provisional application 60/149,396, PCT/US00/08439, PCT/US00/13358, PCT/US00/14042, and US application 10/002,796. For the following reasons, the Examiner finds that the present claims 40-59 are not supported in the manner required by 35 U.S.C. 101 and 112, first paragraph by the prior applications, thus none of present claims is entitled to the benefit of the filling date of the prior applications.

The priority documents 60/149,396, PCT/US00/08439, PCT/US00/13358 merely disclose a polynucleotide sequence of SEQ ID NO:62 encoding a polypeptide of SEQ ID NO:63, which is designated PRO7170, and they fail to provide any specific, substantial and credible utility, nor guidance or working examples to teach how to used the claimed invention. The later PCT/US00/14042, and US application 10/002,796 disclose a working example (Example 61) indicating that the PRO7170 polypeptide was tested positive as either stimulators or inhibitors of glucose or FFA uptake in skeletal muscle, which is determined as insufficient to support a specific and substantial utility for the reasons addressed under ***Objections and Rejections under 35 U.S.C. §101 and §112*** below. Therefore, the Examiner is not able to establish that any of the priority documents satisfies the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph. As such, the claims of the instant application are not entitled to the benefit of the filling date of above prior applications, and the effective filing date for the instantly claimed invention is 02 February 2002, the actual filing date of the instant application.

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 40-59 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 40-59 are directed to an isolated nucleic acid, which has a nucleotide sequence of SEQ ID NO:62, and encodes a polypeptide having an amino acid sequence of SEQ ID NO:63, % variants thereof, fragment thereof encoding the extracellular domain of the polypeptide, and hybridization variants thereof. The encoded polypeptide is designated PRO7170.

The specification discloses a nucleic acid comprising a nucleotide sequence of SEQ ID NO:62, and encoding a human polypeptide PRO7170, having an amino acid sequence SEQ ID NO:63. There is no specific biological significance disclosed in the specification which is directly associated with either the nucleic acid or the encoded polypeptide PRO7170. A working example of detection of polypeptides that affect glucose or FFA uptake in skeletal muscle (Example 61) is noted in the specification, in which PRO7170 polypeptide along with several other polypeptides, were tested positive as *either stimulators or inhibitors* of glucose or FFA uptake (page 143, lines 12-14). Such cannot be used to support a specific and substantial utility for the PRO7170 because the specification does not make it clear whether the PRO7170 stimulates or inhibits glucose or FFA uptake as stimulation and inhibition are mutually exclusive, and both cannot be true. Further, *even if* the PRO7170 were specifically indicated to stimulate or inhibit glucose or FFA uptake in skeletal muscle, it does not constitute an assertion of a specific and substantial utility because it is still unclear whether such an activity is associated with any biological significance, what it can be used for in a "real world", and what well-established utility is associated with the activity.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-59 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility, or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, *even if* the specification taught how to use the PRO7170 polypeptide, enablement would not be commensurate in scope with claims 40-45, 48, 49, and 53-59, which encompass % variants of SEQ ID NO:62 or of a nucleic acid encoding a polypeptide of SEQ ID NO:63 (claims 40-44, for example), hybridization variants thereof under stringent conditions and fragments thereof (claims 53-55), a nucleic acid fragment encoding the extracellular domain SEQ ID NO:63 (claims 48 and 49, for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are directed to % variants, hybridization variants, and fragments of the nucleic acid of SEQ ID NO:62, or of a nucleic acid encoding a polypeptide of SEQ ID NO:63, or the extracellular domain thereof, which read on any or all variants meeting the sequence limitation, and encoding polypeptides either with or without a functional activity. The claims encompass an unreasonable number of nucleic acids encoding inoperative polypeptides. However, the specification provides no guidance or working examples as to how the skilled artisan could use a nucleic acid encoding an inactive polypeptide variant or fragment of SEQ ID NO:63, as no functional limitation is associated with the variants in the claims.

With respect to the fragment of "the extracellular domain", the specification indicates that PRO715 is a secreted protein, and does not define such domain, therefore, it is unclear whether such domain exists, and what kind of functional property it may possess. The

specification provides no guidance or working example as to how to make and use such a fragment.

Further, with respect to the hybridization variants of said nucleotides, the claims read on any or all nucleotides hybridizing to SEQ ID NO:62 or to those encoding SEQ ID NO:63. It is well known in the art that hybridization will occur even under stringent conditions if there is only local identity between two molecules whose sequences might be totally divergent outside of that region. Such hybridized molecules may encode proteins share a common functional property with SEQ ID NO:63, yet have other distinct biological functions from those of SEQ ID NO:63. The specification does not define a specific hybridization condition for obtaining the claimed species, or working examples of any such variants, which would be within the limitations of the claims. Therefore, it would require undue experimentation in order to make and use the claimed invention in its full scope.

Furthermore, with respect to the small nucleotide fragment of 10 nucleotides of said hybridization variant, it may comprise 10 nucleotides which have no sequence homology to SEQ ID NO:62 or to those encoding SEQ ID NO:63. The specification provides no instruction, guidance, or working example regarding such fragments. Clearly, one of skill in the art would not know how to use such a fragment, it would require undue experimentation to practice the invention in a manner commensurate in scope with the claims.

Due to the large quantity of experimentation necessary to determine how to use the nucleic acids encoding inoperative polypeptides, and the small fragments thereof, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which embrace a broad class of structurally diverse variants and fragments, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 40-45, 48, 49, and 53-59 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a nucleic acid having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, SEQ ID NO:62 (claims 40-44), or a nucleic acid encoding a polypeptide of SEQ ID NO:63 (claims 40-44, for example), hybridization variants thereof under stringent conditions and fragments thereof (claims 53-55), a fragment encoding the extracellular domain SEQ ID NO:62 (claims 48 and 49, for example). The claims do not require that the encoded polypeptides possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acids encoding the amino acid sequence set forth in SEQ ID NO:63, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. This is particularly important in absence of a specific known activity. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40-45, 48, 49 and 53 recite the "extracellular domain". However, the protein identified as PRO715 is a soluble protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises the "extracellular domain" is indefinite, as the art does not recognize soluble proteins as having such domains, and the specification does not define such. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain ..., lacking its associated signal sequence" (claim 40, parts (c) and (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

Claim 54 is indefinite because the claims are incomplete for omitting essential elements. The claim is limited by a hybridization method "under stringent conditions". The specification does not define such conditions. As the target sequence is specific, an artisan needs to know the specific corresponding hybridization conditions in order to practice the claimed invention. The claim recites neither hybridization conditions to ensure that any hybridized polynucleotides will

comprise specific sequence within the meaning of the disclosure, nor process steps which would effect the removal of nonspecific hybridization complexes. Without knowing what conditions are comprised by "stringent" conditions, one can not determine the metes and bounds of nucleic acids within the limitations of the claim.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following rejections under 35 U.S.C. §§ 102 and 103 are made in view of the determination that the effective filing date for the instantly claimed invention is 02 February 2002, which is the actual filing date of the instant application.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 40-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Bandman et al. (WO 00/68380).

Bandman disclose a nucleic acid, SEQ ID NO:28, which nucleotide sequence is 99.9% identical to the present SEQ ID NO:62, and encodes a human polypeptide sequence, EXMAD-3 (SEQ ID NO:3), which is 100% identical to SEQ ID NO:63 of the instant application (see computer printout of the search results).

The referenced sequence, therefore, anticipates claims 40-46, 48, 51-55, as being a nucleic acid having at least 80-99% sequence identity to SEQ ID NO:62, or to the sequence encoding the amino acid sequence of SEQ ID NO:63 or of the extracellular domain of SEQ ID NO:63, or hybridizing thereto. Additionally, Bandman teaches an expression vector comprising said nucleic acid, and operably linked to control sequences, and a host cell comprising the vector, wherein the host cell can be E.coli or a yeast cell (page 9, lines 8-10, page 30, lines 17-22, and page 31, paragraphs 2-4), thus, the reference anticipates claims 56-59. With respect to the limitation of "lacking its associated signal peptide" in claims 47 and 49, as the reference teaches the expression of the cited nucleic acid sequence in transfected cells, and the nucleic acid encodes the polypeptide 100% identical to SEQ ID NO:63 of the present invention, such

expression would inherently result in an end polypeptide product having the sequence of SEQ ID NO:63, lacking its associated signal peptide. Thus, the reference also anticipates claims 47 and 49.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Tang et al. (US6,569,662) teaches nucleic acid, SEQ ID NO:17, which comprises nucleotides sequence of the present SEQ ID NO:62 with 99.1% identity (see computer printout of the search results), and encodes a polypeptide (column 3, lines 27-31).

HCGP discloses a nucleotide sequence, locus AW603958 (EST, 23 March 2000), which comprises nucleotides 70-715 of SEQ ID NO:62 of the instant case with 99.2% homology (see computer printout of the search results).

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
6/9/04